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CLINICAL REVIEW

Diagnosis and management of primary hyperparathyroidism

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Primary hyperparathyroidism is the most common cause of hypercalcaemia in the ambulatory setting.[1 2] Although this condition can occur at any age, it commonly affects people over the age of 50 years and postmenopausal women.[2 3] Over the past few decades it has changed from being a condition usually defined by its symptoms to one that is often discovered on routine screening tests while the patient is still largely asymptomatic. In light of advances in research, new guidelines on the diagnosis and management of asymptomatic primary hyperparathyroidism have recently been developed. We review the presentation, diagnosis, and management of primary hyperparathyroidism for the generalist doctor, with evidence drawn from randomised controlled trials, cohort studies, and the most recent consensus guidelines.

Who gets primary hyperparathyroidism?

The exact incidence of primary hyperparathyroidism is not known; however, current data suggest a prevalence of 1-4/1000 in the general population.[1] Women are twice as likely to be affected as men, and most are diagnosed between 50 and 60 years of age.[1-3]

How is calcium regulated?

The four parathyroid glands are situated behind the thyroid gland. Parathyroid hormone (PTH) secreted by the chief cells regulates calcium homeostasis. Decreases in serum ionised calcium are sensed by the calcium sensing receptor on the chief cells, which increase the production and secretion of PTH, thereby enhancing renal tubular calcium reabsorption and osteoclast mediated bone resorption. PTH also enhances the conversion of 25-hydroxyvitamin D_3 into 1,25-hydroxyvitamin D_3, which in turn increases the efficiency of calcium absorption from the bowel.[1] Rising calcium concentrations decrease the release of of PTH, normalising serum calcium values.

What causes primary hyperparathyroidism?

Tumours and hyperplasia

About 85% of cases are caused by a sporadic PTH secreting solitary adenoma of parathyroid chief cells.[1] Multiglandular parathyroid hyperplasia occurs in 1-15% of patients with primary hyperparathyroidism.[1] Parathyroid carcinoma is rare and occurs in less than 1% of cases. Adenomas may be found in ectopic locations in about 16% of cases—commonly the thymus, trachea-oesophageal groove, mediastinum, and the thyroid.[4]

Familial disorders

Primary hyperparathyroidism may also be associated with uncommon familial disorders, including multiple endocrine neoplasia type 1 and type 2A syndromes, familial hyperparathyroidism-jaw tumour syndrome, neonatal severe hyperparathyroidism, and familial isolated hyperparathyroidism. In addition, familial hypocalciuric hypercalcaemia is a benign cause of hypercalcaemia, and it is inherited as an autosomal dominant condition that mimics primary hyperparathyroidism. It is caused by an inactivating mutation of the calcium sensing receptor gene that makes the receptor less sensitive to calcium in the parathyroid glands and the kidneys. Normally, activation of the calcium sensing receptor in the kidney enhances renal calcium clearance. An inactivating mutation leads to decreased sensing of calcium in the kidney and decreased renal calcium clearance, with relative hypocalciuria.[5 6]

Drugs and radiation exposure

Drugs such as thiazide diuretics and lithium may also alter calcium homeostasis. Thiazides may unmask underlying primary hyperparathyroidism because they reduce urinary calcium excretion and can lead to mild hypercalcaemia. Discontinue these drugs if possible and repeat serum calcium (corrected for albumin), PTH, urinary calcium, and creatinine in three months

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Summary points

- Primary hyperparathyroidism (PHPT) is the most common cause of hypercalcaemia in the ambulatory setting; malignancy and other secondary causes must be excluded
- Primary hyperparathyroidism is diagnosed when intact parathyroid hormone is raised or mid to high normal in the setting of raised total or ionised calcium after exclusion of conditions that mimic PHPT
- Medical surveillance comprises annual measurement of serum calcium and creatinine, plus measurement of bone mineral density (at three sites) every one to two years
- Medical management options for select patients and those who do not meet parathyroidectomy guidelines include bisphosphonates and oestrogen replacement (both provide skeletal protection) and the calcimimetic cinacalcet, which can reduce serum calcium and parathyroid hormone values
- Sestamibi imaging is used for localisation before surgery and is not a diagnostic tool—a negative scan does not exclude the diagnosis of PHPT
- Secondary hyperparathyroidism is commonly caused by vitamin D inadequacy or chronic kidney disease

Sources and selection criteria

We searched Medline from 2002 to 2011 using the terms “primary hyperparathyroidism”, “diagnosis”, and “management of primary hyperparathyroidism”. We reviewed all relevant articles as well as the proceedings from the Third International Workshop on Primary Hyperparathyroidism 2008. Articles most relevant to general doctors are presented, including randomised controlled trials, clinical reviews, and cohort studies.

before confirming the diagnosis of primary hyperparathyroidism.[7] Lithium decreases the sensitivity of the calcium sensing receptor to calcium and shifts the set point of the calcium-PTH curve to the right, so that a higher concentration of calcium is needed to suppress PTH release, which leads to increases in serum calcium and PTH.[8] Hence, lithium may also unmask pre-existing parathyroid adenomas or induce parathyroid hyperplasia with prolonged use. Small case series also suggest that a history of radiation exposure to the head and neck may contribute to the development of primary hyperparathyroidism.[9 10]

How do patients with primary hyperparathyroidism present?

Patients with primary hyperparathyroidism may present with symptoms of hypercalcaemia or PTH excess, or they may be asymptomatic, with hypercalcaemia detected incidentally. This last form of presentation is the most common one seen today.

Symptomatic hypercalcaemia

Prolonged increases in PTH lead to the development of symptomatic hyperparathyroidism. Before the implementation of screening laboratory tests in the 1970s, most patients presented with symptomatic primary hyperparathyroidism. Currently, only 20-30% of patients have signs and symptoms of PTH excess at the time of diagnosis in the Western world. However, in developing countries, where biochemical screening is not widely available, most patients still present with symptomatic primary hyperparathyroidism. Symptomatic patients may have fragility fractures or recurrent nephrolithiasis, or both. Other renal manifestations of primary hyperparathyroidism include nephrocalcinosis, polyuria, and renal insufficiency. Patients may also have low bone mineral density, with preferential bone loss at sites rich in cortical bone.[11] Uncommonly, patients develop the classic primary hyperparathyroid bone disease known as osteitis fibrosa cystica. This is characterised by generalised demineralisation of the skeleton, subperiosteal bone resorption, and the development of bone cysts.[11]

Patients with symptomatic hypercalcaemia may also have gastrointestinal symptoms of nausea, peptic ulcer disease, constipation, and pancreatitis. Neurospsychiatric disturbances vary and depend on the severity as well as the rate of rise of serum calcium. Patients may present with depression, lethargy, and decreased cognitive and social function; in those with severe hypercalcaemia, these symptoms may progress to psychosis and coma.[11] Rheumatic conditions such as gout and pseudogout may also be associated with primary hyperparathyroidism.[12] Patients with severe primary hyperparathyroidism may also have left ventricular hypertrophy, cardiac calcification, conduction abnormalities, endothelial dysfunction, and a shortened QT interval. However, the association between mild primary hyperparathyroidism and the development of cardiovascular disease is currently unclear.[13]

Patients with severe hypercalcaemia (>2.75 mmol/L) may present with clinical findings, including volume contraction, muscle weakness, and altered mental status.

Asymptomatic hypercalcaemia

Most patients in the developed world are now diagnosed on routine screening at an asymptomatic stage or during assessment for low bone mineral density. These patients may present with non-specific symptoms of mild hypercalcaemia, such as fatigue, mild depression or malaise.[13]

Normocalcaemic hyperparathyroidism

Patients who present with an incidental finding of raised PTH and normal serum calcium are classified as having normocalcaemic hyperparathyroidism. These patients may present for evaluation of osteoporosis or a fragility fracture and raised PTH is identified on further assessment of the osteoporosis.[13 14] The natural course of normocalcaemic hyperparathyroidism has not been well studied, but prospective observational data suggest that some patients progress to hypercalcaemic hyperparathyroidism.[14] Before confirming this diagnosis, it is essential to exclude vitamin D inadequacy and renal impairment because these conditions may present with increased PTH values and normal serum calcium.

How are patients clinically assessed?

Ask about previous fragility fractures, renal stones, and head and neck irradiation. It is important to exclude other causes of hypercalcaemia, particularly if the serum PTH is not raised, and to exclude occult granulomatous disease (both infectious and non-infectious), thyrotoxicosis, adrenal insufficiency, renal insufficiency, and immobility. An underlying tumour usually

becomes evident before the development of hypercalcaemia. A review of drugs such as thiazide diuretics, vitamin D, vitamin A, absorbable antacids, and lithium is also important. The box outlines the differential diagnosis of PTH and non-PTH mediated causes of hypercalcaemia.

On physical examination, parathyroid adenomas or carcinomas are rarely palpable, although it is essential to search for a palpable neck mass, which is usually caused by coexisting thyroid disease, such as a multinodular goitre.

Which investigations are useful?

In primary hyperparathyroidism, serum calcium is raised and PTH is raised or non-suppressed. About 45% of serum calcium is bound to proteins, mainly albumin, and serum calcium is corrected for albumin using the following calculation: corrected calcium=measured calcium+(40−measured albumin)×0.02, where calcium concentrations are in mmol/L and albumin is in g/L. This formula helps exclude factitious causes of hypercalcaemia. Increased protein binding can occur in patients with hyperalbuminaemia as caused by volume contraction, or rarely in patients with calcium binding paraproteins.[15] In hypercalcaemic patients who have hypoalbuminaemia owing to malnutrition or chronic illness, serum calcium may be falsely normal, but the presence of hypercalcaemia will be confirmed by correcting the serum calcium for albumin. The ionised calcium will also be raised. Measurement of serum ionised calcium also allows exclusion of factitious hypercalcaemia. A low urinary calcium to creatinine clearance ratio helps distinguish between primary hyperparathyroidism and familial hypocalciuric hypercalcaemia, which can also present with raised or high-normal PTH in the presence of hypercalcaemia. In familial hypocalciuric hypercalcaemia, the calcium to creatinine clearance ratio is less than 0.01 in about 80% of patients, whereas in primary hyperparathyroidism it is usually greater than 0.01.[5 15] Consider a diagnosis of familial hypocalciuric hypercalcaemia in patients with relative hypocalciuria, particularly if they are under 25 years. This condition must be excluded before confirming a diagnosis of primary hyperparathyroidism and referring the patient for surgery. Also measure 25-hydroxyvitamin D_3 because patients with primary hyperparathyroidism and vitamin D deficiency may also have a low urinary calcium to creatinine clearance ratio. A persistently low urinary calcium to creatinine clearance ratio after repletion of vitamin D will distinguish between the two conditions.[5]

If the PTH concentration is low, further investigation is needed for non-PTH mediated causes of hypercalcaemia. Investigations to exclude a tumour or occult granulomatous disease are necessary, and initial imaging may include a chest radiograph, a mammogram, a bone scan, ultrasound of the abdomen and pelvis, and serum immunoelectrophoresis. Other non-PTH mediated causes of hypercalcaemia include vitamin D toxicity, adrenal insufficiency, thyrotoxicosis, multiple myeloma, granulomatous diseases such as sarcoidosis, and Paget's disease, particularly in those who are immobilised. Primary hyperparathyroidism can also exist concomitantly with a tumour, which may be causing hypercalcaemia through the release of PTH related peptide, cytokines, or 1,25 dihydroxyvitamin D_3. It is extremely rare for hypercalcaemia to be caused by ectopic secretion of PTH by tumour cells.[15]

Assess renal function because chronic kidney disease can also lead to increases in PTH and result in secondary hyperparathyroidism. In primary hyperparathyroidism and tumours producing PTH related peptide, phosphate values may be low or low-normal owing to the phosphaturic effects of PTH and PTH related peptide. Markers of bone turnover do not need to be measured to confirm a diagnosis of primary hyperparathyroidism Assessment of bone mineral density is useful in evaluating a patient's suitability for parathyroid surgery.[5]

Specialist consultation

Patients are referred to a parathyroid surgeon after the diagnosis of primary hyperparathyrodism is confirmed and their suitability for surgery has been assessed. Before surgery, the parathyroid glands are imaged to guide the surgical approach, localise the adenoma(s), and determine if a minimally invasive approach is feasible. A minimally invasive surgical approach has the benefits of shorter operative time, same day discharge, and a lower rate of complications. Minimally invasive parathyroidectomy is the surgical procedure of choice for localised disease.[16] A total open, four gland exploration is necessary for people with refractory secondary or tertiary hyperparathyroidism, and for those with hyperplasia and recurrent disease.[17]

A recent meta-analysis of the sensitivity and positive predictive value (PPV) of preoperative localisation techniques found that ultrasound had a sensitivity of 76.1% and PPV of 93.2% for localising adenomas (data from 19 studies).[18] Sestamibi scanning had a sensitivity of 78.9% and PPV of 90.7% (data from nine studies). Only two studies investigated four dimensional computed tomography in patients being treated with initial parathyroidectomy, and the results showed a sensitivity of 89.4% and PPV of 93.5%. This study was limited by heterogeneity in disease severity, variability in the size of resected parathyroid glands, a mix of initial and second parathyroid surgery, and the lack of inter-rater reliability of the reporting radiologist in most studies.[18] Importantly, adenoma localisation techniques are not used to confirm the diagnosis of primary hyperparathyroidism. The optimal preoperative localisation technique is best decided in consultation with an experienced parathyroid surgeon.

An initial consultation with an endocrinologist is helpful in confirming a new diagnosis of primary hyperparathyroidism and to ensure that other causes of hypercalcaemia are excluded, in particular familial hypocalciuric hypercalcaemia. Subsequently, a decision can be made by the patient, the endocrinologist, and the general doctor regarding appropriate follow-up care with a specialist or general physician.

How is primary hyperparathyroidism managed with surgery?

According to consensus guidelines, parathyroidectomy is always the definitive treatment for symptomatic hyperparathyroidism in a patient without contraindications to surgery. We focus here on the management of asymptomatic hyperparathyroidism.

Role of parathyroid surgery in patients with mild primary hyperparathyroidism

Parathyroidectomy is always a valuable option in a patient with primary hyperparathyroidism because it normalises serum calcium and PTH. There is reasonable evidence from cohort studies that parathyroidectomy also lowers fracture risk in those with asymptomatic disease.[16] In experienced hands, surgery is of clear benefit. In people with asymptomatic disease who are unwilling or unable to have surgery, medical monitoring with targeted intervention is an attractive option.[19]

Table 1⇓ lists the recommended criteria for parathyroidectomy in patients with asymptomatic primary hyperparathyroidism.

Differential diagnosis of hypercalcaemia[15]

Parathyroid hormone (PTH) mediated

- Primary hyperparathyroidism
- Familial hypocalciuric hypercalcaemia
- Tertiary hyperparathyroidism
- Ectopic PTH production by a tumour

PTH independent

- Cancer: secretion of PTH related peptide, increased calcitriol, bone metastases
- Granulomatous diseases
- Vitamin D intoxication
- Drugs: thiazides, lithium, vitamin A
- Milk alkali syndrome
- Adrenal insufficiency
- Hyperthyroidism
- Immobilisation
- Vitamin A toxicity
- Chronic renal failure

Previous prospective and retrospective studies of patients with mild primary hyperparathyroidism have examined the effects of parathyroidectomy on outcomes such as neuropsychiatric symptoms, nephrolithiasis, heart disease, bone density, and fracture risk. A randomised controlled trial of 191 patients with asymptomatic primary hyperparathyroidism evaluated the effects of parathyroidectomy or medical observation on neuropsychological symptoms.[20] At baseline, all patients had lower quality of life scores on the short form 36 (SF-36) health survey and more psychological symptoms than age and sex matched healthy controls. Although calcium and PTH were normal after surgery in patients randomised to parathyroidectomy, neuropsychiatric symptoms were not better at the two year follow-up.[20] Another randomised controlled trial of 53 patients with mild primary hyperparathyroidism found a benefit of parathyroidectomy in only two of the nine domains of the SF-36 (social function and emotional role) and two of the nine dimensions of a psychometric questionnaire (anxiety and phobia).[21] Collectively, these studies suggest that surgical intervention for mild primary hyperparathyroidism provides minimal benefit for neuropsychiatric symptoms. A randomised controlled trial of 18 patients over 50 years of age with asymptomatic primary hyperparathyroidism aimed to assess improvement in functional capacity and assigned patients to surgery (parathyroidectomy) or control (observation for six months). The six minute walk test was improved in the parathyroidectomy group.[22]

A retrospective cohort study showed that parathyroidectomy decreases the risk of renal stones in primary hyperparathyroidism,[23] and a 10 year prospective cohort study showed that renal stones did not recur in symptomatic patients after a parathyroidectomy.[24] The revised consensus guidelines recommend measuring 24 hour urine calcium to confirm the diagnosis of primary hyperparathyroidism and exclude the presence of familial hypocalciuric hypercalcaemia. This can be done by calculating the calcium to creatinine clearance ratio, either with a "spot" urine after a 12 hour fast or a 24 hour urine collection, which reflects net calcium absorbed from the diet and net calcium bone balance.

In the absence of nephrolithiasis, hypercalciuria with a 24 hour urine calcium greater than 10 mmol/day is no longer an indication for parathyroidectomy because urinary calcium excretion is affected by factors other than the severity of hyperparathyroidism, including age, sex, dietary calcium intake, vitamin D stores, and glomerular filtration rate. A creatinine clearance less than 60 mL/min is an indication for surgery, because impaired renal function may contribute to rises in PTH and progression of the condition.[13]

Preferential bone loss at sites rich in cortical bone has been noted in primary hyperparathyroidism. However, the association between bone mineral density and fracture risk has not been clearly defined in people with asymptomatic disease. A case-control study compared 150 postmenopausal women with primary hyperparathyroidism with 300 controls matched for age and fracture risk.[25] This vertebral fracture assessment study showed a significant increase in vertebral fracture rates in those with primary hyperparathyroidism (24.6% *v* 4%), although most fractures were mild grade compressions. Asymptomatic patients with primary hyperparathyroidism who met the criteria for parathyroidectomy had significantly higher rates of vertebral fracture (28.1% *v* 11.1%).[25] In patients with mild primary hyperparathyroidism, small randomised controlled trials have shown that parathyroidectomy, compared with medical observation, increased bone mineral density at the femoral neck, total hip,[21] and lumbar spine.[26] Those patients with asymptomatic primary hyperparathyroidism who did not meet the criteria for surgery showed no significant difference in fracture rates compared with controls (odds ratio 3.0, 95% confidence interval 1.00 to 8.96; P=0.06). These studies also showed normalisation of serum calcium and PTH with surgery. A retrospective cohort study of 533 patients with primary hyperparathyroidism over the age of 50 years found that parathyroidectomy increased the 10 year fracture-free survival in patients with or without osteoporosis.[27] A meta-analysis found that surgical treatment for mild primary hyperparathyroidism and antiresorptive drugs increase bone mineral density to a similar extent. Patients with untreated mild primary hyperparathyroidism have stable bone mineral density or relatively slow rates of bone loss.[28]

Few studies have examined the effects of parathyroidectomy on cardiac outcomes, particularly in patients with mild primary hyperparathyroidism. A prospective study found that patients with mild primary hyperparathyroidism who had parathyroidectomy had regression of septal hypertrophy.[29] A trial of 116 patients with mild primary hyperparathyroidism randomised to parathyroidectomy or medical observation found no significant difference in mean and diastolic blood pressures or markers of the metabolic syndrome (cholesterol, inflammatory markers, and cardiovascular risk markers) in patients at two

years.[30] Currently, the literature cannot confirm an association between cardiovascular disease and mild primary hyperparathyroidism.

In summary, in experienced hands parathyroidectomy normalises serum calcium and PTH, reduces the risk of fracture, and may provide minor improvement in neurocognitive dysfunction in those with mild primary hyperparathyroidism. Small cohort and retrospective studies suggest that parathyroidectomy reduces the incidence of renal stones. No randomised trials have evaluated the effects of parathyroidectomy on fracture risk. The association between heart disease and mild hyperparathyroidism is also not clear at this time.

How might primary hyperparathyroidism be managed medically?

Medical management is a suitable option in patients who do not meet the guidelines for surgery as well as those who are unwilling or unable to have surgery. Table 2⇓ presents guidelines for monitoring such patients. The efficacy of antiresorptive drugs—oestrogen, bisphosphonates, raloxifene, and cinacalcet—has been evaluated in people with mild primary hyperparathyroidism. All studies were relatively small and not designed to assess effects on fracture risk. In a randomised trial of 26 women with primary hyperparathyroidism, treatment with the bisphosphonate alendronate for two years significantly increased bone mineral density by 8.6% for lumbar spine, 4.8% for total hip, and 1.2% for total body from baseline.[31] Markers of bone turnover such as urinary deoxypyridinoline were also suppressed. A randomised controlled trial of 40 postmenopausal women randomised to receive alendronate or placebo for 48 weeks, followed by treatment withdrawal for 24 weeks, found significant increases in bone mineral density in the treatment arm, with increases at the femoral neck (4.2%) and lumbar spine (3.8%).[32] In a multicentre trial, 44 patients with primary hyperparathyroidism were randomised to placebo or alendronate for 12 months, after which the placebo group was crossed over to active treatment, and all patients were on active treatment in the second year of the study.[33] Treatment with alendronate for two years was associated with a significant increase in lumbar spine bone mineral density (6.8%) compared with baseline. Total hip bone mineral density increased at 12 months and remained stable for the duration of the treatment. Bone mineral density at the distal third of the radius was stable. Reductions in bone turnover markers—urinary N-telopeptide and bone specific alkaline phosphatase—were also noted.[33] These increases are comparable to those seen after parathyroidectomy.

Oestrogen is an effective treatment in postmenopausal osteoporosis. In a randomised controlled trial of 42 women with primary hyperparathyroidism, oestrogen replacement therapy significantly increased bone mineral density from baseline at the total body (1.3%), lumbar spine (5.2%), and femoral neck (3.4%) compared with placebo. Markers of bone turnover, such as alkaline phosphatase, urinary hydroxyproline secretion, and urinary N-telopeptide, were reduced with oestrogen,[34] although it did not lower serum calcium.

Selective oestrogen receptor modulators have tissue specific oestrogen agonist or antagonist effects. In a placebo controlled trial of 18 postmenopausal women with asymptomatic primary hyperparathyroidism, the selective oestrogen receptor modulator, raloxifene, at a dose of 60 mg/day for two months, decreased markers of bone turnover; however, more research is needed to determine whether raloxifene provides skeletal protection in primary hyperparathyroidism.[35 36]

The calcimimetic agent, cinacalcet, decreases calcium and PTH in patients with primary hyperparathyroidism. In a 52 week randomised controlled study of 78 patients, cinacalcet significantly lowered calcium and PTH compared with placebo but had no significant effects on bone mineral density.[37] In the open label extension of this trial, 45 patients with primary hyperparathyroidism were continued on cinacalcet for an additional four years. Cinacalcet decreased serum calcium and PTH but had no significant effect on bone mineral density.[36] Cinacalcet is effective in lowering serum calcium and PTH in those with parathyroid carcinoma and in treating intractable primary hyperparathyroidism and symptomatic hypercalcaemia. Its effects on skeletal protection require further study.

Currently, we have no fracture data for the medical options described above. Fracture data are available after parathyroidectomy from cohort clinical trials.

Conclusion

Primary hyperparathyroidism is usually identified at an asymptomatic stage in the Western world. Many advances have been made in the diagnosis and the surgical and medical management of this condition. Surgery is always a valuable and appropriate treatment option. Medical monitoring with targeted medical intervention is also suitable for select patients and for those who do not meet the revised surgical guidelines for parathyroidectomy.

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Additional educational resources

Resources for healthcare professionals

Khan AA, Bilezikian JP, Potts JT Jr. The diagnosis and management of asymptomatic primary hyperparathyroidism revisited. *J Clin Endocrinol Metab* 2009;94:333-4—Good general summary

Bilezikian JP, Khan AA, Potts JT Jr. Guidelines for the management of asymptomatic primary hyperparathyroidism: summary statement from the third international workshop. *J Clin Endocrinol Metab* 2009;94:335-9

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Resources for patients

UpToDate (www.utdol.com). Patient information: primary hyperparathyroidism. The basics and beyond—A succinct summary of content patients may find useful in understanding the symptoms and management of their disease

Calcium Disorders Clinic (www.stjosham.on.ca/calcium)—Link to a specialised clinic in the management of calcium disorders and parathyroid disease.

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Tables

Table 1| Guidelines for parathyroidectomy in asymptomatic primary hyperparathyroidism19

Measurement	Criteria
Serum calcium	>0.25 mmol/L above upper limits of normal
24 hour urine calcium	Not indicated
Calculated creatinine clearance	<60 mL/min
Bone mineral density	T score of −2.5 or less at any site or previous fragility fracture (or both)
Age	<50 years

Table 2| **Guidelines for medical surveillance in asymptomatic primary hyperparathyroidism19**

Measurement	Recommendations
Serum calcium	Annually
Serum creatinine	Annually
Bone mineral density	Every 1-2 years
Abdominal radiography (with or without ultrasound)	Not recommended
24 hour urine calcium	Not recommended
Creatinine clearance (24 hour urine collections)	Not recommended